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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/815,341	03/22/2001	Nancy J. Bump	BBC-069	4413

7590 11/21/2005  
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EXAMINER

SMITH, CAROLYN L

ART UNIT PAPER NUMBER

1631

DATE MAILED: 11/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Advisory Action  
Before the Filing of an Appeal Brief**

Application No.

09/815,341

Applicant(s)

BUMP ET AL.

Examiner

Carolyn L. Smith

Art Unit

1631

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 24 October 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 4 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☒ The Notice of Appeal was filed on 24 October 2005. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: \_\_\_\_\_.  
Claim(s) objected to: \_\_\_\_\_.  
Claim(s) rejected: 21-27, 32 and 33.  
Claim(s) withdrawn from consideration: 1-20, 28-31 and 34-88.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

Continuation of 11. does NOT place the application in condition for allowance because: Applicants' arguments have been considered but are unpersuasive for the reasons discussed below. Consequently, the 35 USC 112, 1st paragraph, rejections (lack of scope of enablement and lack of written description) and the 35 USC 103 (a) rejections are maintained.

**35 USC 112, 1st paragraph, lack of scope of enablement rejection**

Applicants' summarize the rejection. Applicants' maintain previously set forth arguments. Examiner maintains already set forth response to those unpersuasive arguments. Applicants summarize the Drenth article which demonstrates the unpredictability in the trial and error procedures performed in the protein crystallization science. Applicants argue that Drenth states a standard procedure for crystallizing a protein. This statement is found unpersuasive as it is well known to be a science involving unpredictability which does not make it a routine procedure. Applicants state they have provided crystallization conditions in their specification to enable one skilled in the art to make crystals. Again, it is reiterated that Applicants have successfully provided enablement for atomic coordinates for residues 802-1124 of Tie-2 and Inhibitor complex, but does not provide enablement for the atomic coordinates of an unbound version of a Tie-2 polypeptide or atomic coordinates of the complete polypeptide of Tie-2 and Inhibitor complex. Due to the unpredictability in this art, only atomic coordinates specifically mentioned in the originally filed disclosure are enabled.

**35 USC 112, 1st paragraph, lack of written description rejection**

Applicants summarize the rejection. Applicants argue that the catalytic domain of Tie-2 (residues 802-1124) must be present in order for a compound to inhibit the Tie-2 protein, so that it doesn't matter whether the unbound or entire Tie-2 polypeptide and inhibitor complex is being used. This is an allegation without factual support. It is well known in the art that compounds change shape and configuration depending on their bound or unbound state. Applicants have demonstrated that they had possession at the time the invention was filed of the catalytic domain of Tie-2 according to the atomic coordinates specifically recited in the originally filed disclosure. Applicants mention the "comprising" terminology. Because this terminology encompasses other atomic coordinate possibilities, besides those specifically set forth in the specification, these other atomic coordinate possibilities lack adequate written description.

**35 USC 103(a) rejection**

Chen et al. in view of In re Gulack

Applicants argue that obtaining crystal coordinates is one of the steps in the instant invention. It is noted that instant claim 21 recites obtaining atomic coordinates. Applicants argue that the atomic coordinates of the crystal are functionally related to the method of claim 21 because the atomic coordinates identify the active subsites of Tie-2, which in turn allows one to identify or design an inhibitor of Tie-2. This statement is found unpersuasive as coordinates do not actively play a role which alters computer system functionality.

Chen et al. in view of In re Gulack and In re Best and In re Fitzgerald and Ziegler

Applicants note that their previous arguments regarding Ziegler's extracellular domain and Applicants' catalytic domain of Tie-2. It is reiterated that the instant claims do not state the compound must bind to the catalytic domain of Tie-2, instead the compound must bind to one or more active sites. Applicants refer to page 3, lines 21-25 of their specification. While claims are to be read in light of the specification, it is noted that limitations of the specification are not to be directly read into the claims unless those limitations are specifically set forth in the claims. Applicants are encouraged to read their claims carefully to understand that their claims do not specifically state the compound must bind to the catalytic domain.

Chen et al. in view of Vikkula et al. and In re Best and In re Fitzgerald

Applicant argues similar arguments as above that the compound must bind to the catalytic domain. Careful reading of the claims would reveal that the compound does not have to bind to the catalytic domain of Tie-2, instead the compound must bind to one or more active sites. It is noted that an "active site" may be broadly construed to be any binding site on a protein, and it is not specifically defined by the instant specification to be a catalytic domain. Applicants' arguments are deemed unpersuasive.

**MARJORIE A. MORAN**  
**PRIMARY EXAMINER**

*Marjorie A. Moran*  
11/9/05